227. *Substitution in Compounds containing Two or More Phenyl Groups. Part IV. Nitration of Diphenyl Derivatives containing* m-*Directing Substituents.*

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Many examples are known, notably in the naphthalene series, in which the deactivating influence of a *m*-directing substituent in one ring of a polycyclic system induces further substitution by a kationoid reagent to take place in a second ring (cf. Ingold, *Ann. Reports*, 1926, **23**, 134; Lapworth and Robinson, *Mem. Manchester Phil. Soc.*, 1928, **72**, 50, *et seq.*). In the diphenyl series, apart from the nitration of 2- and 4-nitrodiphenyl (Schultz and Strasser, *Ber.*, 1881, **14**, 612; Bell and Kenyon, J., 1926, 2705; Gull and Turner, J., 1929, 491), and of 3-nitrodiphenyl (Blakey and Scarborough, J., 1927, 3000), which give rise exclusively to heteronuclear substitution, there is practically no information available on the introduction of a single substituent into a derivative containing one *m*-directing group. The nitration of diphenyl derivatives containing other typical *m*-directing groups, such as ·CO·R (R = H, CH_3, or OH), should be of particular interest since such groups, while being predominantly *m*-directing, nevertheless in the benzene series give relatively high proportions of *o*-substitution as well, which has been attributed in part to the initial attachment of the reagent to the side chain.

A simple general method has now been developed for the mononitration of 4-acetyldiphenyl, diphenyl-4-aldehyde, and diphenyl-4-carboxylic acid, involving the use of nitric acid of strength approximating to the composition HNO_3,H_2O, at — 5° to 0°. Unless these conditions are closely adhered to, either no action at all, or dinitration will result (with or without oxidation in the case of the aldehyde and ketone). This general procedure has also been extended to the nitration of 4- and 2-nitrodiphenyl, as well as to the dinitration of diphenyl.

The mononitration of diphenyl-4-carboxylic acid was attempted by Gull and Turner (*loc. cit.*), who, using fuming nitric acid (*d* 1·5), were able to obtain only dinitrated products. The diphenylcarboxylic acid is largely insoluble in the weaker acid here employed, but, nevertheless, under these conditions it is converted into 4- and 2-nitrodiphenyl-4′-carboxylic acid in almost equal proportion. The former acid was identical with that previously obtained from the oxidation of 4-nitro-4′-methyldiphenyl (J., 1932, 1891), and the latter with that similarly obtained from 2-nitro-4′-methyldiphenyl and also by independent synthesis (*ibid.*, p. 1892). The high-melting 4-nitrodiphenyl-4′-carboxylic acid was also identified by the preparation and mixed melting point of its *ethyl* ester.

In similar manner, nitration of diphenyl-4-aldehyde gave 4- and 2-*nitrodiphenyl-4′-aldehyde*, and nitration of 4-acetyldiphenyl gave 4-nitro-4′-acetyldiphenyl and 2-*nitro-4′-acetyldiphenyl*. Both pairs of compounds were identified by oxidation to the corresponding carboxylic acids. Kuhling (*Ber.*, 1895, **28**, 523) has described an aldehyde and a ketone, which he regarded as 4-nitrodiphenyl-4′-aldehyde (m. p. 115—120°) and 4-nitro-4′-acetyldiphenyl (m. p. 90—94°). It is obvious that these compounds are different from those described here, which melt respectively at 127° and 152—153°, and from their method of preparation it seems highly probable that they are either mixtures or the corresponding 4 : 2′-isomerides. This confusion has been definitely proved for Kuhling's "4-nitro-4′-methyldiphenyl" (*Ber.*, 1895, **28**, 41; 1896, **29**, 166; Kliegl and Huber, *ibid.*, 1920, **53**, 1655; Gomberg and Pernert, *J. Amer. Chem. Soc.*, 1926, **48**, 1379), as well as for his "4-nitrodiphenyl-4′-carboxylic acid" (J., 1932, 1891, footnote), which are actually 4-nitro-2′-methyldiphenyl and 4-nitrodiphenyl-2′-carboxylic acid respectively.

The further nitration of 4-nitrodiphenyl-4′-carboxylic acid has already been described (J., 1932, 1892), and for comparison that of 4-nitro-4′-acetyldiphenyl was carried out. With fuming nitric acid at 0° 2 : 4′-*dinitro-4-acetyldiphenyl* was obtained; at higher temperatures oxidation to 2 : 4′-dinitrodiphenyl-4-carboxylic acid took place as well.

The nitration of diphenyl-4-carboxylic acid and -4-aldehyde and 4-acetyldiphenyl has thus shown that in all three cases, substitution occurs mainly, if not exclusively, at the 2′- and 4′-positions, just as with 4-nitrodiphenyl, and in no case has any homonuclear substitution product been isolated. It has been shown by Baker and Moffitt (J., 1931, 314) that the proportions of the isomerides formed in the nitration of an aromatic aldehyde or ketone depend to a certain extent on the conditions of nitration, and that in particular the presence of concentrated sulphuric acid appreciably increases the proportion of *m*-substitution. Since the nitration of the above diphenyl derivatives was carried out in the absence of sulphuric acid, the non-formation of any appreciable amount of homonuclear substitution products is the more remarkable.

Experiments were also carried out on the application of the Friedel–Crafts reaction to 2- and 4-nitrodiphenyl. Although, *e.g.*, nitrobenzene undergoes extensive combination with aluminium chloride, and nitro-compounds in general are not susceptible to the Friedel–Crafts reaction, nevertheless it seemed reasonable to expect that these diphenyl derivatives might undergo some acylation in the non-nitrated nucleus, if a large excess of aluminium chloride were employed. The preparation of 4-nitro-4′-acetyldiphenyl from 4-nitrodiphenyl and acetyl chloride in the presence of aluminium chloride in over 50% yield is now described, as well as the preparation of 2-*nitro-4′-acetyldiphenyl* from 2-nitrodiphenyl in similar manner. The products were identical with those obtained from the nitration of 4-acetyldiphenyl, and were further identified by oxidation to the corresponding carboxylic acids.

The Orienting Power of the Phenyl Group.—The phenyl group has long been established as belonging to the *op*-directive class of aromatic substituents, but until recently no definite evidence was available with regard to its effect on velocity of substitution. Previous qualitative results on the nitration of methyldiphenyls (J., 1932, 1888, 2245, 2636) have indicated that the phenyl group, like methyl, gives rise to increased reactivity towards further nuclear substitution by kationoid reagents. Additional evidence in support of this view is now found in the fact that benzene may be employed with advantage as an almost inert solvent, in place of the more usual carbon disulphide, in the preparation of 4-acetyldiphenyl from diphenyl by means of the Friedel–Crafts reaction. Diphenyl-4-aldehyde has also been prepared from diphenyl in benzene solution (Gattermann, *Annalen*, 1906, **347**, 381; Hey, J., 1931, 2476). The close correspondence between the results of the nitration of 3-methyldiphenyl (J., 1932, 2245) and those on substitution in 1 : 3-diphenylbenzene, recently carried out by Wardner and Lowy (*J. Amer. Chem. Soc.*, 1932, **54**, 2510) and by Cook and Cook (*ibid.*, 1933, **55**, 1212), also confirms the analogy between the phenyl and the methyl group as activating groups in aromatic substitution. Further, the formation of chains of several phenyl groups when diphenyl and its derivatives are prepared by the method of Gomberg and Bachmann (*J. Amer. Chem. Soc.*, 1924, **46**, 2341) and Gomberg and Pernert (*ibid.*, 1926, **48**, 1372), as well as their formation from diazotised aniline, as described by Gerngross and Dunkel (*Ber.*, 1924, **57**, 739), also indicates an unusually high reactivity at the *p*-position to a phenyl group in an aromatic nucleus.

EXPERIMENTAL.

Derivatives of 4-*Acetyldiphenyl*.—4-Acetyldiphenyl has been prepared from diphenyl by means of the Friedel–Crafts reaction in carbon disulphide solution (Adam, *Ann. Chim. Phys.*, 1886, **15**, 224; Ferriss and Turner, J., 1920, 1147; Gull and Turner, J., 1929, 498). Better results were obtained by using benzene as solvent. Acetyl chloride (50 g.) was gradually added to diphenyl (50 g.) in benzene (100 g.) in the presence of aluminium chloride (70 g.) cooled in ice water. The reaction proceeded gently and during the later stages the mixture became warm and viscous. After several hours, crushed ice and benzene were added, and after separation of insoluble material, the benzene layer was washed with dilute sodium hydroxide and with water. Evaporation of the benzene left a solid residue to which was added the material previously isolated by filtration, and the whole was heated to 230°, 14 g. of practically pure acetophenone being collected. The residue (m. p. 110—115°, 45 g.), recrystallised from acetone or alcohol, gave pure 4-acetyldiphenyl, m. p. 120—121°.

Nitration experiments. (*a*) 4-Acetyldiphenyl was added gradually to fuming nitric acid (*d* 1·50) at 0°. After standing, the product was precipitated by pouring into water, and crystallisation from aqueous alcohol gave 2 : *4′-dinitro-4-acetyldiphenyl* in pale yellow needles, m. p. 155—156° (Found: N, 9·7. $C_{14}H_{10}O_5N_2$ requires N, 9·8%). On oxidation by means of potassium permanganate, as described below, this gave 2 : 4′-dinitrodiphenyl-4-carboxylic acid (m. p. and mixed m. p. 256°).

(*b*) No action occurred on addition of 4-acetyldiphenyl to a mixture of fuming nitric acid and acetic acid, or to nitric acid (*d* 1·42) at 0°, but on raising the temperature oxidation as well as nitration took place. Treatment with nitric acid (*d* 1·46) at room temperature gave a mixture of mono- and di-nitration products.

(*c*) 4-Acetyldiphenyl (4 g.) was added gradually to well-stirred nitric acid (100 c.c., *d* 1·46) at −5° to 0°. After 15 mins. the clear solution was poured into water and the precipitated solid filtered off. By repeated crystallisation from alcohol two main fractions were obtained: (i) m. p. 147—151° (3·2 g.) and (ii) m. p. 86—96° (1·4 g.). Further crystallisation of fraction (i) gave pure 4-nitro-4′-acetyldiphenyl (m. p. and mixed m. p. 152—153°), while fraction (ii) gave *2-nitro-4′-acetyldiphenyl* in small prisms, m. p. 110° (Found: N, 5·75. $C_{14}H_{11}O_3N$ requires N, 5·8%). The mononitration was quantitative.

Oxidation. A suspension of 4-nitro-4′-acetyldiphenyl (2 g.) in boiling water was treated with potassium permanganate (5 g.), added in 6 portions at ½-hour intervals. After 2 hours' further boiling, the mixture was filtered and the filtrate treated with sulphur dioxide. The precipitated acid, after crystallisation from alcohol, had m. p. 336—338°, both alone and on admixture with 4-nitrodiphenyl-4′-carboxylic acid (J., 1932, 1891).

Oxidation of 2-nitro-4′-acetyldiphenyl in similar manner gave 2-nitrodiphenyl-4′-carboxylic acid, m. p. and mixed m. p. 250° (J., 1932, 1892).

Nitration of 4-*Nitro-4′-acetyldiphenyl*.—(*a*) 4-Nitro-4′-acetyldiphenyl was heated on the steam-bath for 10 mins. with fuming nitric acid (*d* 1·50), and poured into water; the precipitated solid, which was soluble in aqueous alkali, gave 2 : 4′-dinitrodiphenyl-4-carboxylic acid (m. p. and mixed m. p. 256°) on crystallisation from alcohol.

(*b*) 4-Nitro-4′-acetyldiphenyl (5 g.) was added to well-stirred fuming nitric acid (100 c.c., *d* 1·50) at 0°, and after 1 hour the clear solution was poured into water. Crystallisation of the precipitated solid from aqueous alcohol gave 2 : 4′-dinitro-4-acetyldiphenyl (m. p. and mixed m. p. 155—156°).

The Friedel–Crafts Reaction on 4- *and on* 2-*Nitrodiphenyl*.—The preparation of 4-nitro-4′-acetyldiphenyl in small yield from 4-nitrodiphenyl by means of the Friedel–Crafts reaction was carried out by Dilthey, Neuhaus, Reis and Schommer (*J. pr. Chem.*, 1930, **124**, 124). The following conditions have been found to give a yield of 55%. Acetyl chloride (24 g.) was added gradually with frequent shaking to a mixture of 4-nitrodiphenyl (20 g.), aluminium chloride (80 g.), and carbon disulphide (300 c.c.). No appreciable amount of reaction took place until the mixture was heated to 45—50°, at which temperature it was maintained for 10 hours. The dark-coloured product was poured into water, and the brownish solid which separated was filtered off and refluxed with benzene. (Evaporation of the carbon disulphide layer in the filtrate left only a trace of residue.) The benzene extract was filtered and dried, and on evaporation left a light brown solid (m. p. 145—147°, 14 g.). After two crystallisations from benzene or alcohol, 4-nitro-4′-acetyldiphenyl was obtained in pale yellow prisms, m. p. 152—153°, which on oxidation, as previously described, gave 4-nitrodiphenyl-4′-carboxylic acid.

The preparation of 2-nitro-4′-acetyldiphenyl was carried out in the same manner from 2-nitrodiphenyl (20 g.). The dark oil (13 g.) obtained from the benzene extract did not solidify. By distillation under reduced pressure, a pale yellow oil was collected (b. p. 225—230°/8 mm., 10 g.), which solidified on cooling. Crystallisation, first from benzene–light petroleum and then from aqueous alcohol, afforded 2-nitro-4′-acetyldiphenyl in small prisms, m. p. 110°, which on oxidation, as already described, gave 2-nitrodiphenyl-4′-carboxylic acid.

Derivatives of Diphenyl-4-*aldehyde*.—The aldehyde was prepared by the modification of Gattermann's method previously described (J., 1931, 2476).

Nitration experiments. (*a*) Diphenyl-4-aldehyde was added to well-stirred nitric acid (*d* 1·46), and the mixture warmed until solution took place. The solid, which separated on pouring into water, consisted mainly of 2 : 4′-dinitrodiphenyl-4-carboxylic acid (m. p. and mixed m. p. 256°).

(*b*) The aldehyde (3·5 g.) was added to well-stirred nitric acid (40 c.c., *d* 1·46) at −5° to 0°, and after 15 mins. the mixture (containing solid in suspension) was poured into water. The precipitated solid on crystallisation from alcohol gave two main fractions: (i) less soluble, m. p. 125—130° (2·5 g.); (ii) more soluble, m. p. 80—85° (1·2 g.). The former fraction appeared to be contaminated with a small quantity of a higher-melting impurity, but by repeated crystallisation 4-*nitrodiphenyl*-4′-*aldehyde* was obtained in pale yellow needles, m. p. 127° (Found : N, 6·0. $C_{13}H_9O_3N$ requires N, 6·2%). Further crystallisation of fraction (ii) gave 2-*nitrodiphenyl*-4′-*aldehyde* in microscopic crystals, m. p. 101° (Found : N, 6·1. $C_{13}H_9O_3N$ requires N, 6·2%). On warming the mother-liquors with acetone and a few drops of sodium hydroxide solution, there was no indication of the formation of an indigotin derivative. Both nitrodiphenyl aldehydes were oxidised by means of alkaline permanganate, as described for the oxidation of the nitro-ketones, to give the corresponding carboxylic acids, which were identified by m. p. and mixed m. p.

Derivatives of Diphenyl-4-*carboxylic Acid*.—Diphenyl-4-carboxylic acid was obtained either from the aldehyde, or from 4-acetyldiphenyl by oxidation with alkaline permanganate, as described by Gull and Turner (*loc. cit.*).

Nitration experiments. (*a*) Diphenyl-4-carboxylic acid was added to well-stirred nitric acid (*d* 1·46) at −5° to 0°. Since no dissolution took place, the temperature was gradually raised until a clear solution was obtained, which was then poured into water. The precipitated solid consisted mainly of 2 : 4′-dinitrodiphenyl-4-carboxylic acid (m. p. and mixed m. p. 256°).

(*b*) Diphenyl-4-carboxylic acid (4 g.) was added gradually to well-stirred nitric acid (100 c.c., *d* 1·46) at −5° to 0°. After 15 mins.' stirring, water was added, and the precipitated solid filtered off and extracted with boiling alcohol. A portion dissolved, the solution yielding 2-nitrodiphenyl-4′-carboxylic acid (m. p. and mixed m. p. 250°, 2·1 g.), while the much less soluble residue consisted of 4-nitrodiphenyl-4′-carboxylic acid (m. p. and mixed m. p. 238—240°, 2·4 g.). The ethyl ester of the latter was prepared by heating a solution of the acid in 5% alcoholic hydrochloric acid on the steam-bath for 2 hours. When cold, the crude ester was filtered off, and after two crystallisations from aqueous alcohol, *ethyl* 4-*nitrodiphenyl*-4′-*carboxylate* was obtained in pale yellow needles, m. p. 112° (Found : N, 5·25. $C_{15}H_{13}O_4N$ requires N, 5·2%).

The standard method of procedure for the mononitration of 4-acetyldiphenyl, diphenyl-4-aldehyde, and diphenyl-4-carboxylic acid, *viz.*, treatment with well-stirred nitric acid (*d* 1·46) at 0° for 15 mins., was also applied to 4- and 2-nitrodiphenyl and to diphenyl itself. Both nitrodiphenyls were quantitatively mononitrated, and the diphenyl quantitatively dinitrated.

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